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TrippBio, Redefining the Treatment of Respiratory Viruses

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CEOCFO: ***Dr. Martin, the first thing I see on the TrippBio, Inc site, big and bold, is "Imagine a world where we control COVID 19." What is your plan for doing so at TrippBio?***
Dr. Martin: We have identified a compound based on work from Dr. Ralph Tripp and his lab at the University of Georgia. He has been working on a program to identify compounds that have antiviral activity, but were not originally designed as antiviral agents, essentially looking to repurpose drugs. As far back as 2013, he published a paper on the effect of Probenecid inhibiting influenza A. It showed very potent activity in inhibiting that particular RNA virus.

Fast forward to last year, when the SARS-CoV-2 virus hit. He looked at the virus and decided to test probenecid against it and was somewhat surprised by how potent it was at suppressing the virus. The University then turned around and licensed the program to a company called SpinUp Campus, which then formed TrippBio. That is the basis for the work that we are doing. We are currently positioning ourselves to move into clinical trials by evaluating our proprietary formulation of Probenecid, what we call TD-213, as a treatment against SARS-CoV-2 infection and in particular treating mild to moderate disease. We have in vitro antiviral activity and in vivo data in hamsters that show very potent activity. This data was recently posted to a pre-print server a couple of weeks ago.

CEOCFO: ***Why does it work? How does it work? Do we know?***
Dr. Martin: We believe we know. Probenecid inhibits a host factor, so it targets something within the individual itself, rather than targeting the virus, which is a very important distinction, because drugs that are directly acting antivirals have a high rate of resistance development. That is true with Tamiflu as well as the newer drug that came out a couple of years ago, Xofluza.

By inhibiting a host factor, we are able to bypass the typical way that the virus can mutate around the drug activity. Therefore, what we believe TD-213 is doing is inhibiting a cellular process in which the virus hijacks the intercellular machinery and uses it, repurposes it within the cell, to produce viral proteins. We believe that TD-213 blocks a very critical step in that viral processing pathway and essentially stops viral assembly and replication prior to the infectious virus being produced.

CEOCFO: ***What has been the response from members of the medical community that are aware of what TrippBio has and what you have been working on and developing?***
Dr. Martin: The response to the scientific data that we have been published has been overwhelmingly positive. The work out at Dr. Tripp's lab is top notch. He is a former section chief at the CDC responsible for corona virus research at the CDC, so his antiviral work is stellar and well respected. The issues that we have, the concerns around therapeutic drug development now, is not so much the scientific in "will this work." The in vitro data clearly says that it will work. There

has just been some questioning of, "Do we need a therapeutic since these vaccines are working so well." My emphatic answer to that is yes, we do!

CEOCFO: ***Why is that?***
Dr. Martin: It is very simple. One, not everybody is going to get vaccinated. We know that for sure. You can listen to any of the media reports. Right now, we are hovering around 50 60 percent of the United States population being vaccinated, although it varies widely across individual states. Most of the projections that I have seen would suggest that between 20 and 30 percent of individuals eligible for a vaccine will not take the vaccine, for a variety of different reasons. In addition, we do know that there are breakthrough infections that can occur even with vaccination.

The CDC published some data just recently, looking at these so-called breakthrough infections, and while the numbers are relatively low, it is important to note in the data that roughly 2 percent of patients that became infected with SARS-CoV-2 and got sick with COVID 19, ultimately died. This is about a 10-to-20-fold higher mortality rate than with the common flu. Vaccines, while they are very effective, are not going to be a cure-all. Therefore, you need to have very effective treatments to be used in the event of an infection, either in an un-vaccinated individual or in an individual that has been vaccinated.

CEOCFO: ***Would the rates of people vaccinated in other countries be much less as well?***
Dr. Martin: Absolutely! The aforementioned comment really just focused on the US. If you go outside of the US and, I would say, outside of Europe as well, the rates of vaccination are significantly lower and the timeline to get vaccines to those countries is significantly prolonged. Therefore, having an effective, relatively inexpensive medication to treat the signs and symptoms of COVID 19 and prevent hospitalizations and ultimately prevent deaths would be significant.

"We have a compound that we believe could really revolutionize the treatment of respiratory infections caused by viruses. We have a very broad-based activity across a number of different viruses; COVID 19, influenza, Respiratory Syncytial Virus and when someone gets an infection this fall, they get a runny nose or the sniffles, it could be COVID 19, if could be influenza, it could be RSV, a drug like TD-213 could be useful for any of those infections." Dr. David E. Martin

CEOCFO: ***You are looking at proof of concept studies. When will they start and what will be involved?***
Dr. Martin: For proof of concept, we are looking to do studies in patients with mild to moderate COVID 19, on an outpatient basis. Our primary endpoints will be symptoms while the viral end points, hospitalizations and mortality will be secondary end points. However, the objective of that initial first proof of concept study will be to look at a couple of different dose levels and determine what is the most effective, safest dose that can be administered and then use that data to plan our registration studies.

CEOCFO: ***As you are repurposing something that existed, will it be easier to get approval as you go forward?***
Dr. Martin: Nothing is ever easy to get approved by the FDA, but what I would say is the regulatory pathway is a little bit simpler and more streamlined for a repurposed drug. You can go through what is known as the 505(b)(2) regulatory pathway, which we are planning to do, which does minimize the amount of additional non-clinical work that we have to do and then can potentially reduce some of the clinical studies that we have to do.

I do think that COVID 19 is a special beast, if you will. It is not clear to me what the regulatory landscape will look like next year when we have completed our initial study, whether emergency use authorization will be possible or we will have to go through a full registration Phase 2/3 study package. Much of it depends on how effective some of the other drugs that are found to be investigated are and what the pandemic looks like after this upcoming flu season, which I think could be quite significant.

CEOCFO: ***What have you learned so far that might have surprised you?***
Dr. Martin: The thing that I have learned is looking at all of the repurposing literature that is out there. One of the things that shocks me is that, certainly early on in the pandemic, everyone was looking for anything at all that had any kind of activity against SARS-CoV-2 and they were touting those as potential cure-alls. There was a lot of, I do not want

to say misinformation, but rather incorrectly understood information, that was out on a number of repurposed drugs. The implications of that are, when you do good science, even with excellent in vitro data and good animal data, we are still having to overcome some of the intrinsic biases against repurposed drugs from some of the information that came out last year.

I would say that for us, there is a bit of skepticism with the drug and the potency that we are seeing for TD-213 since it is significantly better than many of the new chemical entities currently being investigated by large pharma. It was recently announced that the government is buying a very large shipment of Merck's investigational agent. What I would say about that is; our drug, if you look at them side by side, we are actually much more potent in vitro than that compound is. However, because it is a so called new chemical entity, people look at that, I think, more favorably. Therefore, we are swimming a bit upstream with repurposing something like TD-213.

CEOCFO: ***What is your situation regarding funding? It is always a challenge.***
Dr. Martin: It is always a challenge. We are always trying to raise money and that is what we are currently doing. In addition to the activity against COVID 19, we have very potent activity against influenza and Respiratory Syncytial Virus (RSV). Therefore, we are looking to raise money to fund the development programs for all three of those indications. We have just as good a potency against those other 2 viruses as we do with SARS-CoV-2 virus. We think that, in many respects, influenza and RSV are much more attractive markets and are well underserved by current treatments.

CEOCFO: ***Would you tell us about RSV?***
Dr. Martin: Respiratory Syncytial Virus is a very common upper respiratory virus that infects almost everyone. The numbers are such that by the age of 2 almost every newborn has been infected at least once with RSV. It is a ubiquitous virus. The very young infants, typically less than 6 months old or the very elderly or immunocompromised, can be quite susceptible. It is one of those viruses that, for someone who is normal and healthy, there is almost no negative to effects to the infection. They just have a little bit of a cold. However, for someone that is more immunocompromised or elderly or very, very young; they can get quite sick. It is a leading cause of hospitalization among the elderly and in infants and has a very high mortality rate.

There are really no currently available therapeutics that are useful. There is an old antiviral drug called Ribavirin that is used, but the clinical data supporting its use is somewhat questionable. The only other drugs are monoclonal antibodies that are used in neonates for prophylaxis, basically to help prevent one of the newborns at high risk from getting the infection. However, there are really no treatment options available for patients.

CEOCFO: ***Do most people even know about it?***
Dr. Martin: Not really. It is not one of those viruses that, unless someone has been infected with it and has been hospitalized. If you get a cold during the winter months, the odds are fairly high that you may have RSV. However again, in people with relatively normal immune systems, it is not going to be a problem. For people that have underlying immune related conditions or underlying respiratory conditions, it can be quite deadly.

CEOCFO: ***Are people paying more attention to the flu due to COVID? Or is it more under the radar just because COVID is taking precedence over everything else?***
Dr. Martin: I think to some extent that COVID has certainly risen to the forefront of everyone's mind over the last 18 months. There is a fair amount of literature now looking at this. The flu season, last year, was very mild and everyone pretty much agreed that the reason it was mild was because everyone was wearing a mask and every one was socially distanced. In those instances, the flu did not spread wildly like it normally does.

People really did not think a lot about the flu last year, because it just was not around, because everyone was doing the risk mitigation for COVID 19. I think what is going to be particularly problematic is this winter. Vaccination rates are quite high, all of the restrictions are being eased, no one is wearing a mask out in public these days and there are not any real restrictions around social gathering and social distancing. Therefore, it is very likely that the flu will come back with a vengeance.

There is some question about how virulent the flu virus may be this year, given that it kind of skipped a year in terms of being spread around. However, I think that it is quite likely that we are going to see an intersection of these respiratory

viruses with people infected with both influenza and potentially COVID 19 at the same time and we are going to begin seeing some spikes and deaths attributable to both of those viruses this fall and winter.

CEOCFO: ***How are you reaching out to potential investors, perhaps partners? What have you learned over the years that might help you in getting what you need?***
Dr. Martin: I think the bottom line is that you have to know you audience. You have to know who you are reaching out to. Is the group that you are talking to interested in therapeutics? That may seem obvious but, some investment groups only do diagnostics. Some investment groups only invest in programs that are in Phase 2 or Phase 3 or they have a specific therapeutic focus that does not include respiratory diseases. Therefore, I think you have to know your audience. Then, you have to be able to tailor a message that can grab their attention relatively quickly and keep their attention, so in a limited amount of time you get their mind share.

At the end of the day, after you have made your best case, it is really up to them whether they want to invest or not. You have to talk to lots of people and not everyone is going to find your idea attractive. Not everyone is going to be willing to make the leap. However, all it takes is 1 or 2 investors to get interested and once you get that, I will never say that the money comes easily after that, but it is more straightforward to get money in, once you have got one or two interested investors.

CEOCFO: ***Why pay attention to TrippBio?***
Dr. Martin: We have a compound that we believe could really revolutionize the treatment of respiratory infections caused by viruses. We have a very broad-based activity across a number of different viruses; COVID 19, influenza, Respiratory Syncytial Virus and when someone gets an infection this fall, they get a runny nose or the sniffles, it could be COVID 19, if could be influenza, it could be RSV, a drug like TD-213 could be useful for any of those infections.

By taking drug treatment relatively early in the course of the infection, it is possible that you could avoid some of the long-term effects of the long COVID syndrome that is starting to come out and be more obvious, now that a number of people have survived the infection. We think we have got a drug that can treat that and that can potentially prevent some of those long-term symptoms coming. We are looking at it in a relatively short course of therapy, so one pill to treat a number of different viruses could be quite useful.